CBER Update

The Orange County Regulatory Affairs (OCRA) Discussion Group
June 16, 2005
Irvine, California

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Deputy Director, Operations

Center for Biologics Evaluation and Research

Vision for CBER

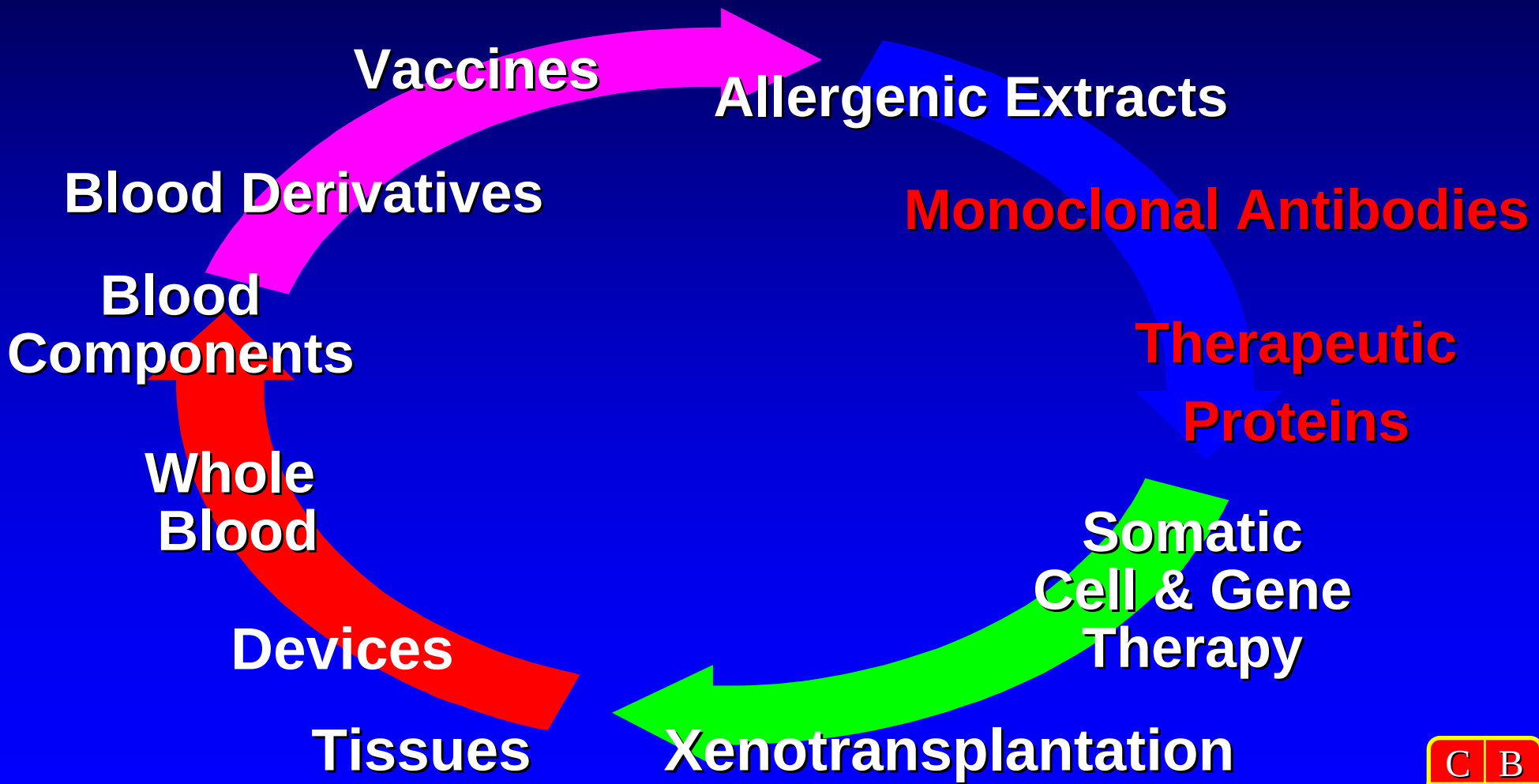
Innovative Technology
Advancing Public Health

Protect and improve public and individual health in the US, and if possible, globally

Facilitate development, approval and access to safe and effective products

Strengthen CBER as preeminent regulatory Agency for biologics

Biological Products



What Went

- Monoclonal antibodies
- Cytokines, growth factors, enzymes, interferons -- (including recombinant versions)
- Proteins intended for therapeutic use that are extracted from animals or microorganisms (except clotting factors
- Other therapeutic immunotherapies

What Stayed

- **Monoclonal antibodies, cytokines, growth factors, or other proteins when used solely as an *ex vivo* constituent in a manufacturing process / when used solely as a reagent in the production of a product that is under the jurisdiction of CBER**
- **Viral-vectored gene insertions (i.e., "gene therapy")**
- **Products composed of human or animal cells or from physical parts of those cells**

Personnel Updates

- OCTGT: Dr Celia Witten selected as Director
- OCBQ:
  - Mary Malarkey selected as Director
  - Gil Conley selected as Director, Division of Inspections and Surveillance
  - OVRR: Dr. Norman Baylor appointed Director
- OBRR:
  - Dr. Jonathan Goldsmith, Deputy Director
  - Dr. Susan Abbondanzo, Deputy Director, DH
- OBE: Director search underway

Reinvention of Device Review: Continuing Success Supported by MDUFMA: 510k Review Time Performance

Receipt to Final Action-FY 2002-FY 2005**

	MDUFMA			
	FY02	**FY03**	**FY04**	**FY05***
CBER Review Time (days)	**119.1**	**58.7**	**64.0**	**58.5**
Average Number of Cycles	**1.7**	**1.3**	**1.3**	**1.0**

Includes SEs/NSEs/WDs

*Data through January 31, 2005

The Regulatory Pendulum

Centralization

Enforcement

Legal emphasis

Privatization

Process

Decentralization

Education

Science-based

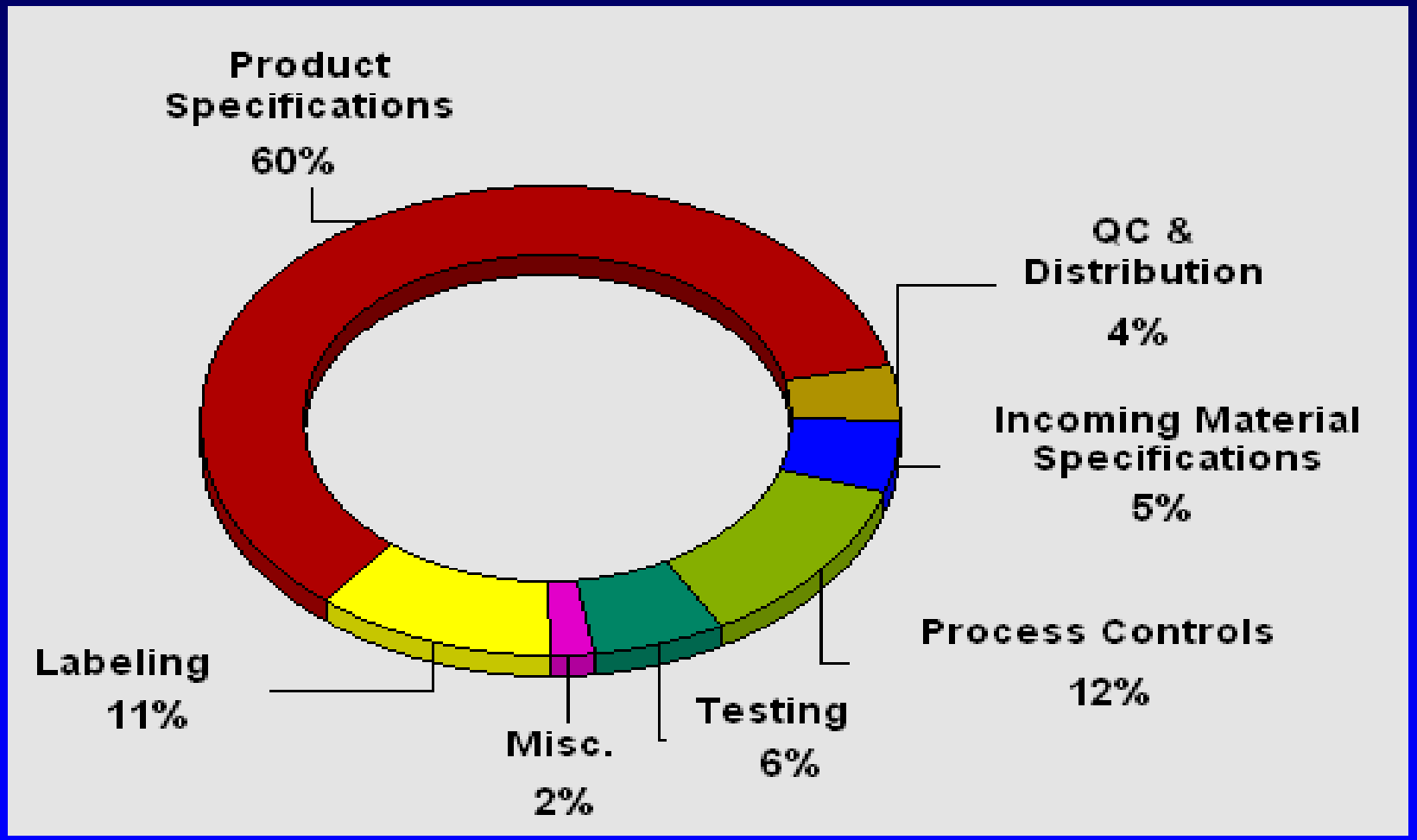
Government

Content

FDA Inspections for Biologics Products Who Does What?

- **Depending on the type of inspection: CBER, Team Biologics, or District Office may conduct the inspection**
- **Products regulated by CBER - CBER will conduct the PLI/PAIs; Team Biologics will conduct routine GMP inspections**
- **Team Biologics - performs routine GMP inspections for biologics products (CBER and CDER), product specialists participate**

FY04 Biological Product Deviation Reports – Non-Blood



Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach

- FDA initiative announced in August 2002
- Two-year + program
- Applies to pharmaceuticals, including biological human drugs and veterinary drugs (excludes blood/plasma)
- Steering Committee comprised of CBER, CDER, CVM, CDRH*, CFSAN*, ORA, and the Office of the Commissioner

Revolution or Evolution?

A slide from a 1998 presentation

TEAM BIOLOGICS

- A plan for Reinventing FDA's Ability to Optimize Compliance of Regulated Biologics Industries
  - Joint effort of CBER and the Office of Regulatory Affairs
- Capitalize on diverse skills and knowledge
- Focus on inspectional and compliance issues

Final Report

- **Issued September 29, 2004**
- **Key accomplishments:**
  - **Quality Systems model for Agency operations**
  - **Quality Systems guidance for CGMP regulation**
  - **Adoption of risk management principles**
  - **Risk-based pharmaceutical quality assessment system**
  - **Development of science-based policies**
- **http://www.fda.gov/cder/gmp/gmp2004/GMP_finalreport2004.htm**

Compliance-Related Accomplishments

- Part 11
- Dispute Resolution
- Comparability Protocols
- Aseptic Processing

Aseptic Processing Guidance

Objectives

Update the 1987 aseptic guidance

Reflect changes in industry technologies and methods

- **Promotes drug quality**
  - **Clear and consistent communication of regulatory expectations in guidance promotes voluntary compliance with FDA regulations**
  - **Improve clarity where needed and on issues of most concern**
- **Based on current science**
- **Encourages innovation**
  - **Encourage and facilitate technological advancements**
  - **Automation and enhanced product protection are key themes**
  - **Liberalizes some old standards**

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Background
Aseptic Processing: Risk-based Approach

- **In accord with 21st Century initiative and Strategic Plan, new guidance incorporates risk-based CGMP approaches throughout**
  - **e.g., environmental monitoring, media fills, design**
- **Prevention…**
  - **updated guidance facilitates compliance, and thus helps avert product quality issues**
  - **a firm's quality system should detect emerging hazards**

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Background
Development of the guidance

- **Previous Guidance……..1987**
- **Concept Paper Issued……...Sept. 27, 2002**
- **Advisory Committee Meeting…….Oct. 22, 2002**
- **PQRI Recommendation……Mar. 5, 2003**
- **Draft Guidance Issued…….....Aug. 22, 2003**
- **Final Guidance Published…….Sept. 29, 2004**

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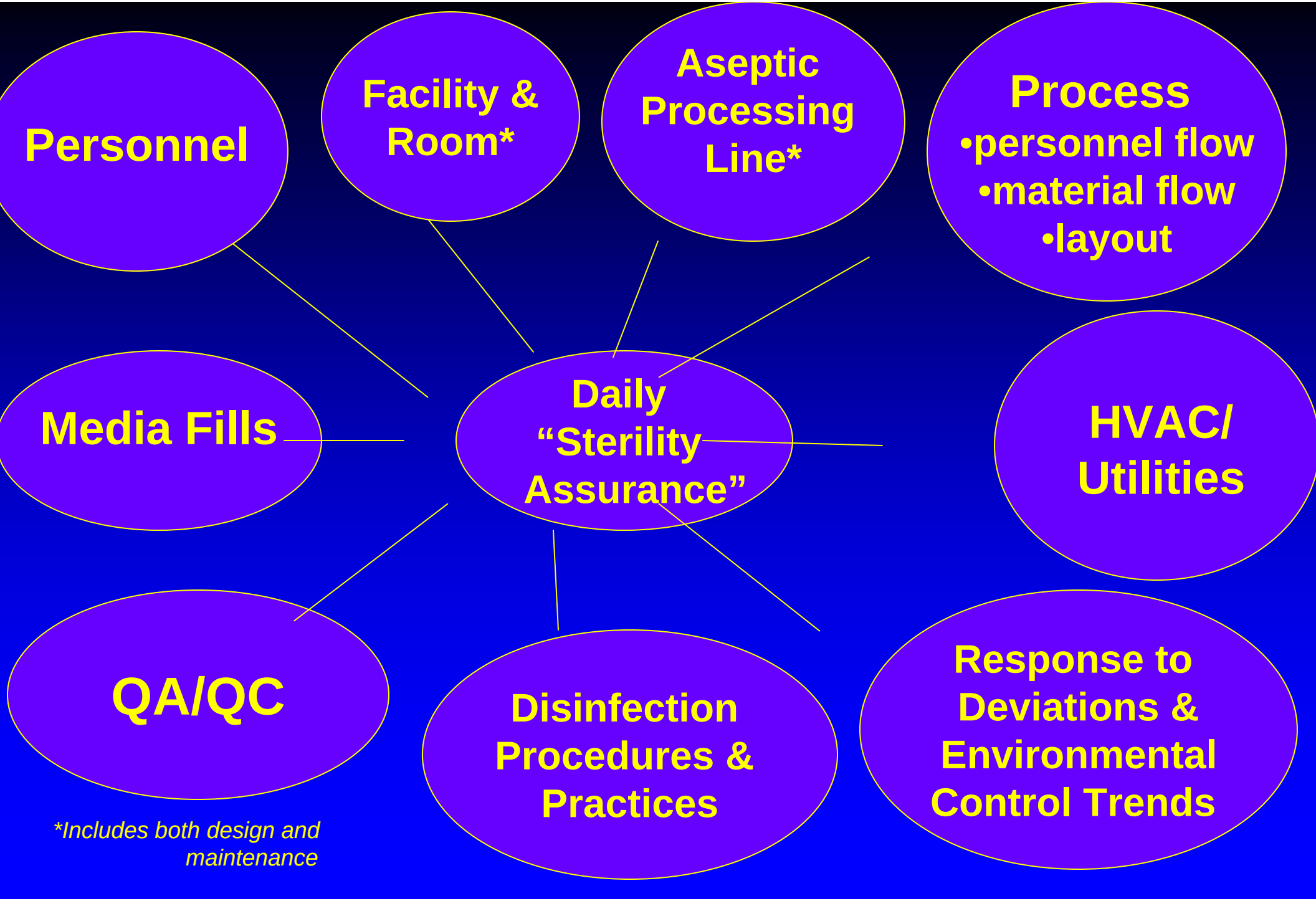
Background
Public Comments

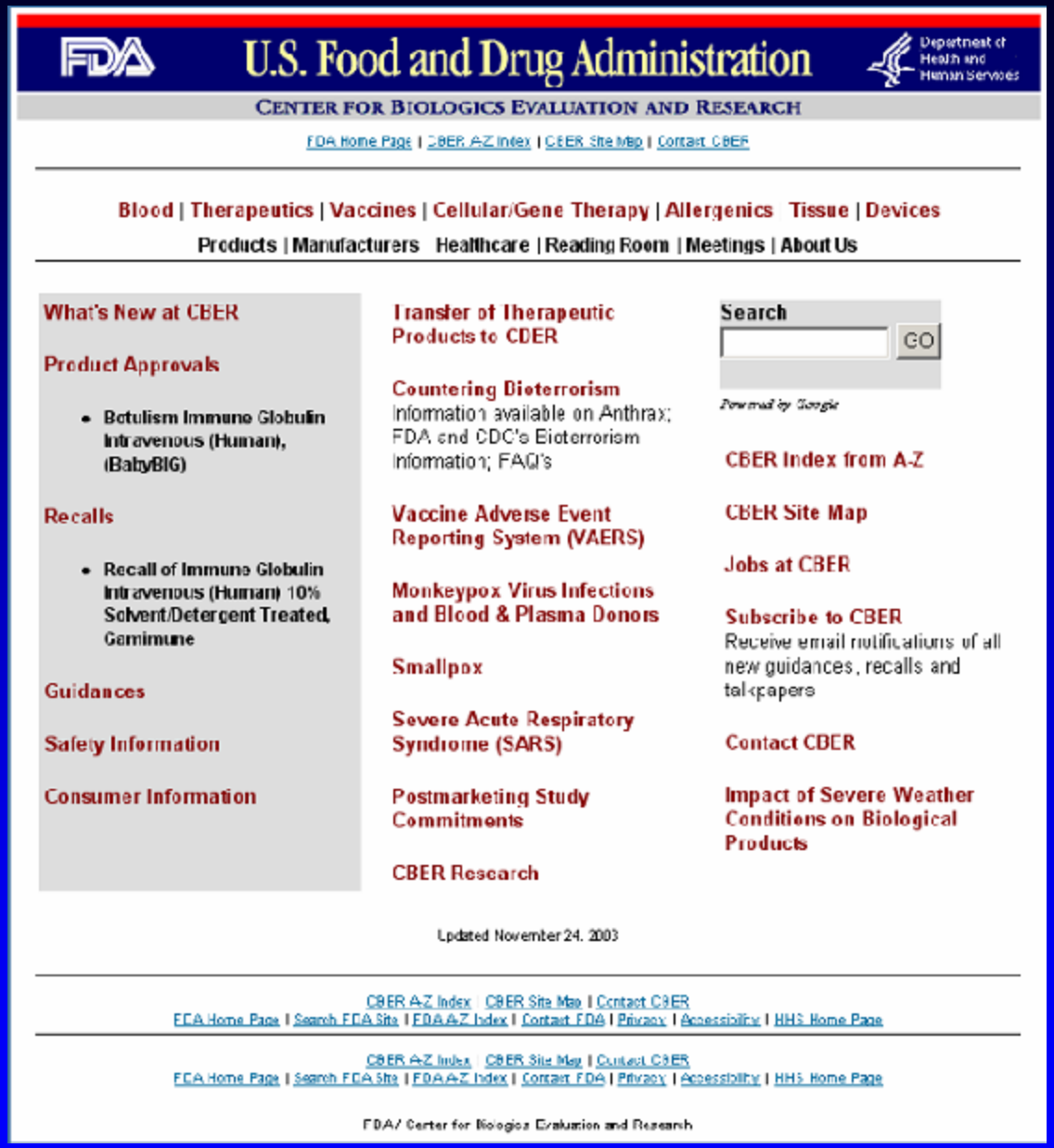
- **Product of extensive outreach to industry and academia**
- **60-day comment period**
- **61 parties submitted comments to the docket**
- **Over 1800 individual comments**
  - **recommended text modifications**
  - **many introductory comments from industry and organizations**
  - **many comments were repeated (sometimes verbatim)**
  - **several technical issues had comments on both sides of matter**
  - **workgroup incorporated numerous changes based on the public comments**

Aseptic Processing Workgroup Members

Final revision team: CDER/ CBER/ ORA

- **Susan Bruederle, ORA**
- **Robert Coleman, ORA**
- **Kris Evans, CDER/OC**
- **Rick Friedman, CDER/OC**
- **Joe Kutza, CDER/OPS**
- **Bob Sausville, CBER/OCBQ**
- **Marla Stevens-Riley, CDER/OPS**
- **Paul Stinavage, CDER/OPS***
- **Brenda Uratani, CDER/OC**


Personnel
Facility & Room*
Aseptic Processing Line*
Process
•personnel flow
•material flow
•layout
Media Fills
Daily "Sterility Assurance"
HVAC/ Utilities
QA/QC
Disinfection Procedures & Practices
Response to Deviations & Environmental Control Trends
*Includes both design and maintenance



FDA U.S. Food and Drug Administration

Department of Health and Human Services

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What's New at CBER

Product Approvals

- Botulism Immune Globulin Intravenous (Human), (BabyBIG)

Recalls

- Recall of Immune Globulin Intravenous (Human) 10% Solvent/Detergent Treated, Gamimune

Guidances

Safety Information

Consumer Information

Transfer of Therapeutic Products to CDER

Countering Bioterrorism
Information available on Anthrax; FDA and CDC's Bioterrorism information; FAQ's

Vaccine Adverse Event Reporting System (VAERS)

Monkeypox Virus Infections and Blood & Plasma Donors

Smallpox

Severe Acute Respiratory Syndrome (SARS)

Postmarketing Study Commitments

CBER Research

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Impact of Severe Weather Conditions on Biological Products

Updated November 24, 2003

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We're Here to Help You!

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